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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,380	04/01/2002	Fabrizio Samaritani	P/42-63	7114

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 08/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	10/009,380	SAMARITANI ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 7/13/04 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *13 July 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1-15*.

   Claim(s) withdrawn from consideration: _____.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Continuation of 5. does NOT place the application in condition for allowance because: Claims 1-3, 6-10, 13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Fabbri et al., US Patent No. 5,017,557 in view of Samaritani, WO 95/35116. The basis for this rejection is set forth at pages 2-4 of the last Office Action (13 January 2004). The rejection has been maintained for reasons of record.

Applicant states that the Fabbri patent relates to GRF but does not teach or suggest the use of saccharose in a GRF composition. Applicant maintains that there is no reference to stabilization in this patent although there is a reference to a composition comprising mannitol as an excipient. Applicant states that Fujioki does not teach or suggest that saccharose can be used as an effective stabilizer for GRF. Applicant argues that the Tarantino reference fails to teach or suggest the use of saccharose as a stabilizer. Applicant states that Samaritani teaches that saccharose can stabilize HGH but does not teach or suggest that it can stabilize any other protein. Applicant states that what requires stabilization in GRF is Met at position 27, Asp at position 3, the Asp-Ala bond at connecting positions 3-4 and Asn at position 8. Applicant argues that the record does not establish that HGH has these amino acids at these positions and therefore, the fact that saccharose may stabilize HGH does not provide any basis it will stabilize GRF. Applicant argues that at the very best, these assertions teach saccharose might possibly be a stabilizer for proteins and that possibility should be explored.

Applicant states that Tables 1-3, formulations 1 and 2 contain mannitol while formulation 3 contains saccharose. Applicant maintains that Table 2 shows that with mannitol, the pH increased over the 4 weeks of the study whereas the formulation containing saccharose did not increase from the initial value. Applicant states that Table 3 shows that the peptide purity of the mannitol containing compositions decreases by about 2% or more over the 4 weeks of the study whereas the saccharose containing formulation lost only 0.2% over the same period of time. Applicant states that the fact that saccharose provided a stability which is better than mannitol stabilized GRF is clearly surprising and unexpected when viewed in light of the conclusion in the Office Action that native GRF or GRF plus mannitol would be expected to behave in the same manner as with saccharose.

Applicant's arguments have been fully considered but not deemed persuasive because the formulations employed almost twice the amount of saccharose (34.2 mg/ml) than mannitol (18.2 mg/ml) (see page 4, Table 1 formulation 1 and formulation 3). Thus the fact that the pH of the formulation containing saccharose did not increase from the initial value and lost only 0.2% of peptide purity over the same period of time, is not surprising and unexpected. Saccharose and mannitol are both sugars. Saccharose, like mannitol are known protein stabilizer in the art. It would be obvious to one skilled in the art to try a similar stabilizer, such as saccharose. A formulation using twice the amount of protein stabilizer would provide better stability. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claims 1, 4, 5, 11 and 12 remain rejected under 35 U.S.C. 103(a) as beingunpatentable over Fabbri et al., US Patent No. 5,017,557 in view of Samaritani, WO 95/351 16 and Fujioka et al., US Patent No. 4,963,529. The basis for this rejection is set forth at page 4 of the last Office Action (13 January 2004).The rejection has been maintained for reasons of record.

Applicant incorporates their response to the rejection in the arguments above. Applicant's arguments have been fully considered but are not found to persuasive for the reasons discussed above in the maintained rejection in 35 USC 103(a).

Claims 1, 2, 13, 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fabbri et al., US Patent No. 5,017,557 in view of Samaritani, WO 95/35116 and Tarantino, US Patent No. 5,863,549.The basis for this rejection is setforth at page 5 of the last Office Action (13 January 2004).The rejection has been maintained for reasons of record.

Applicant incorporates their response to the rejection in the arguments above. Applicant's arguments have been fully considered but are not found to persuasive for the reasons discussed above in the maintained rejection in 35 USC 103(a).